REMARKS/ARGUMENTS

Claims 1-5 and 30-63 are active. Claims 6-29 have been withdrawn from consideration and now are cancelled without prejudice. The claims have been revised to conform to U.S. practice, for clarity and to reduce claim fees. New claims 42-48 refer to different compounds for component (B) and find support in claim 1. New claims 49-53 refer to the elected species and new claims 54-63 find support in original claim 4. No new matter is believed to have been added. Favorable consideration of the remarks below and allowance of this case is respectfully requested.

Election of Species/Election

The Applicants previously elected with traverse the following combination of species:

(i) compound with neuropeptide Y (NPY) receptor affinity: **2-[4-(8-methyl-2-oxo-4H-benzo[d][1,3]oxazin-1-yl)-piperidyn-1-yl]-N-(9-oxo-9H-fluoren-3-yl)acetamide hydrochloride;**

(ii) compound with 5-HT6 receptor affinity: **N-3-(2-dimethylaminoethyl)-1H-indol-5-yl]-5-chloronaphthalene-2-sulphonamide; and**

(iii) a use: **regulation of appetite.**

The Applicants understand that additional species will be rejoined and examined upon an indication of allowability for a generic claim reading on the elected species. The Applicants respectfully request that the claims of the nonelected group(s) or other withdrawn subject matter which depend from or otherwise include all the limitations of an allowed elected claim, be rejoined upon an indication of allowability for the elected claim, see MPEP 821.04.

Request for Compact Examination

The Applicants note that this case and U.S.10/566,402 are under examination by the same Examiner and request consolidation of prosecution to expedite prosecution as well as the identification of allowable subject matter.

Provisional Rejection--Obviousness-type Double Patenting

Claims 1-5 and 30-41 were provisionally rejected under the judicially-created doctrine of obviousness-type double patenting over claims 1, 2, 4-9, 34 and 35 of copending application U.S. 10/566,402. PAIR indicates that the copending application has not been allowed (status 09-15-2010, Final Rejection Mailed). Both of these applications were filed July 29, 2004 and the copending application has not been allowed. The Applicants submit that the foregoing amendments and remarks address all the remaining rejections and place this application in condition for allowance. Accordingly, this provisional double patenting rejection can be withdrawn, MPEP 804(I)(B). If necessary, this issue will be addressed during prosecution of the copending application.

Provisional Rejection--Obviousness-type Double Patenting

Claims 1, 3, 4 and 30 were provisionally rejected under the judicially-created doctrine of obviousness-type double patenting over claims 22 and 29 of copending application U.S. 10/565,979, in view of Jover, et al., U.S. 2004/0058920 and further in view of Merce-Vidal, et al., U.S. 7,105,515 and Caldirola, et al., U.S. 7,144,883. According to PAIR the copending application was allowed on September 30, 2010 but has not yet issued as a patent. Allowed claims 22 and 29 are distinguishable from the pending claims because the pending claims require a combination of (A) and (B), where (B) is (B) is at least one compound with 5-HT_6

receptor affinity selected from the group consisting of the benzoxazinone-derived sulfonamide compounds of general formula (Ib), (Ic), (Id), (Ie), (If), (Ig), and (Ih). Component (B) is not described in the claims 22 and 29 of the allowed copending application and the rejection sets forth no reasoning why the combination of (A) and (B) would have been obvious to those of ordinary skill in the art. Accordingly, this rejection cannot be sustained.

Provisional Rejection--Obviousness-type Double Patenting

Claims 1, 3, 4 and 30 were provisionally rejected under the judicially-created doctrine of obviousness-type double patenting over claims 1 and 19-23 of copending application U.S. 10/566,399, in view of Merce-Vidal, et al., U.S. 7,105,515 and Caldirola, et al., U.S. 7,144,883. The copending application has not been allowed and its status as of 01-08-2010 is "Non-final Action Mailed" according to PAIR. The Applicants submit that the foregoing amendments and remarks address all the remaining rejections and place this application in condition for allowance. Accordingly, this provisional double patenting rejection can be withdrawn, MPEP 804(I)(B).

Rejection--Obviousness-type Double Patenting

Claims 1, 3-5 and 30 were rejected under the judicially-created doctrine of obviousness-type double patenting over claims 22 and 29 of U.S. Patent No. 7,056,914, in view of Jover, et al., U.S. 2004/0058920 and further in view of Merce-Vidal, et al., U.S. 7,105,515 and Caldirola, et al., U.S. 7,144,883. This rejection cannot be sustained because the secondary references provide no motivation or direction for producing the combination of the invention.

Rejection--Obviousness-type Double Patenting

Claims 1, 3-5 and 30 were rejected under the judicially-created doctrine of obviousness-type double patenting over claims 1 and 3 of U.S. Patent No. 7,041,665, in view of Jover, et al., U.S. 2004/0058920 and further in view of Merce-Vidal, et al., U.S. 7,105,515 and Caldirola, et al., U.S. 7,144,883. This rejection cannot be sustained because the secondary references provide no motivation or direction for the combination of the invention.

Rejection--Obviousness-type Double Patenting

Claims 1, 3-5 and 30 were rejected under the judicially-created doctrine of obviousness-type double patenting over claims 1-7 of U.S. Patent No. 7,514,429, in view of Merce-Vidal, et al., U.S. 7,105,515 and Caldirola, et al., U.S. 7,144,883. This rejection cannot be sustained because the secondary references provide no motivation or direction for the combination of the invention.

Rejection—35 U.S.C. §112, first paragraph

Claims 1-5 and 30-41 were rejected under 35 U.S.C. 112, first paragraph, lacking adequate enablement for solvates. While not necessarily agreeing with the basis for the rejection since solvate formation is well known in the art and can be performed without undue experimentation, this rejection is now moot in view of the removal of that term from the claims. The Applicants also note that paragraphs [0727] and [0728-0757] on pages 123-135 describe methods for making and using the composition of the invention, such as how to administered or formulate the composition of claim 1. Accordingly, no undue experimentation would have been required to practice the invention as now claimed.

Rejection—35 U.S.C. §112, second paragraph

Claims 1 and 3-5 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite. This rejection is moot in view of the amendments above, including the removal of the term "medicament" and the clarification of the claims as product (composition) claims.

Rejection—35 U.S.C. §101

Claims 4-5 were rejected under 35 U.S.C. 101 as being non-statutory claims. This rejection is now moot in view of the revision of these claims in accordance with U.S. practice.

Rejection—35 U.S.C. §112, second paragraph

Claims 4-5 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite. This rejection is also moot in view of the amendment of these claims. The method claim 5, for example, now recites a step of administering the composition to a subject in need thereof.

Rejection—35 U.S.C. §112, first paragraph

Claims 1-5 were rejected under 35 U.S.C. 112, first paragraph, lacking adequate written description. This rejection may be withdrawn in view of the amendments above which remove the term "medicament" and revise the claims in standard method of treatment claim format.

Rejection—35 U.S.C. §103

Claims 1-5 and 30-33 were rejected under 35 U.S.C. 103 as being unpatentable over Jover, et al., U.S. 2004/0058920 and further in view of Merce-Vidal, et al., U.S. 7,105,515 and Caldirola, et al., U.S. 7,144,883. This rejection cannot be sustained because the cited

references provide no motivation for making the specific combination of components (A) and (B) of the invention nor any reasonable expectation of success for the superior pharmacological properties of this combination.

The primary reference, Jover, is relied upon for teaching a genus containing a benzooxazinone compound of component (A) of general formula (1a) for use as a medicament (OA, top of page 20), including oral medicaments, and for teaching that neuropeptide Y receptor regulators are useful for regulation of food intake (OA, bottom of page 20) as powerful stimulants of food ingestion. The Examiner states at the top of page 21 of the OA that such neuropeptide Y regulators significantly increase appetite when neuropeptide Y is directly injected to the CNS of satiated mice.

At the bottom of page 21 of the OA, the Examiner acknowledges that Jover does not teach component (B) of the invention, a 5-HT6 receptor affinity compound. Since Jover does not teach this element it cannot provide any motivation for combining this element with component (A) of the invention or provide a reasonable expectation of success for the combination of components (A) and (B) of the invention.

To teach what is missing from Jover, the Examiner relies on Merce-Vidal and Caldirola.

Merce-Vidal is asserted to teach sulphonamides of formula (I) depicted at the bottom of page 21 of the OA and to read on the elected species of component (B) when the particular substituents describes at the top of page 22 of the OA are present.

Caldirola is cited as teaching substitutes sulfonamide compounds with 5-HT6 receptor affinity for treatment of medical conditions including obesity, type II diabetes and disorders of the central nervous system, OA, 2nd paragraph on page 22.

In her statement of the *prima facie* case for obviousness in the section of the OA bridging pages 22-23, the Examiner states:

> One having ordinary skill in the art would have been motivated in making such a medicament combination in expectation of using the same in a method for treating CNS disorders. One of ordinary skill in the art would have been motivated to incorporate the two agents herein in a single combination pharmaceutical composition because combining the agents herein each of which is known to be useful to treat depression individually into a single combination is prima facie obvious.

Initially, it is worth noting that none of the cited references, Jovan, Merce-Vidal, or Caldirola, provide any express motivation for combining components (A) and (B). Therefore, the first prong of the test in *In re Vaeck*, 20 USPQ2d 1438 (Fed. Cir. 1991), that the references themselves or the knowledge in the art must provide some suggestion or motivation to arrive at the invention has not been met. Moreover, as the Supreme Court recently stated, "*there must be some articulated reasoning* with some rational underpinning to support the legal conclusion of obviousness." *KSR Int'l v. Teleflex Inc.*, 127 S. Ct. 1727, 1741 (2007) (quoting *In re Kahn*, 441 F.3d 977, 988 (Fed. Cir. 2006) (emphasis added)). Here, the Examiner has not articulated any reason why one of ordinary skill in the art would have selected the combination of an agonist for an NPY receptor and an agonist for $5HT_6$ receptor as opposed to compositions containing only one of these agonists or combinations of either agonist with other compounds. Those of skill in the medical arts would have understood the unpredictability of what effects would occur when different types of medications are mixed. Here, the Examiner has not explained why the combination of an agonist for an NPY receptor and an agonist for $5HT_6$ receptor would have been recognized as safe and effective by those of ordinary skill in the pharmaceutical or medical arts.

The Examiner also refers to the decision in *In re Kerkhoven*, 205 USPQ 1069, 1072 (CCPA 1980) to support a prima facie case for obviousness. This case states "It is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... ", MPEP 2144.06. As noted above, there was no reasonable expectation of

success in the prior art for the safety and efficacy of the combination of the invention. However, even setting that aside, *Kerkhoven* is **not** on point with the present invention due to significant underlying differences in the subject matter in *Kerkhoven* (detergent compositions) and the subject matter of the invention (agonists that recognize different receptors and have different biological activities).

In *Kerkhoven*, the court held that a process for preparing a detergent mixture ("mixed-active detergents") by spray drying two conventional detergents (an anionic detergent and a non-ionic detergent) together was *prima facie* obvious absent evidence of unexpected results. The *Kerkhoven* invention involved mixing two detergents which each have the same basic mechanism of detergent action. A detergent, whether anionic or non-ionic, has hydrophobic and hydrophilic components which permit it to dissolve or emulsify both hydrophilic and hydrophobic materials. On the other hand, the invention involves different classes of compounds with affinity for NPY receptor or affinity for $5HT_6$ receptor which have different biological mechanisms of action.

Unlike the detergent mixture in *Kerkhoven* there was no reasonable expectation of success that mixing compounds (A) and (B) which recognize different types of receptors would have produced a third composition having the same effects as either compound (A) or compound (B) alone. For example, it was well-known that mixing different classes of drugs may result in antagonism, where the biochemical mechanism of one drug interferes with the biochemical mechanism mediating the effect of the other drug.

On the other hand, the inventors have discovered that the combination of (A) a compound with affinity for NPY receptor and (B) a compound with affinity for the $5HT_6$ receptor surprisingly exhibit synergy and exert greater effects compared to the individual components, see e.g., page 421 of the specification. Such synergy would have been surprising to one of ordinary skill in the art because each drug was known to interact with a

different type of receptor. The prior does not suggest or provide a reasonable expectation of success for combining (A) a compound with affinity for NPY receptor and (B) a compound with affinity for the $5HT_6$ receptor to achieve the affects recognized by the inventors, such as synergy and reduced side-effects.

Consequently, since the prior art provides no motivation for combining these references, any reasonable expectation of success that the composition of the invention would be efficacious and safe, or any suggestion of the synergy of the claimed combination, this rejection cannot be sustained.

Rejection—35 U.S.C. §103

Claims 34-41 were rejected under 35 U.S.C. 103 as being unpatentable over Jover, et al., U.S. 2004/0058920 and further in view of Merce-Vidal, et al., U.S. 7,105,515 and Caldirola, et al., U.S. 7,144,883, and further in view of Noda, et al., U.S. 5,320,853. This rejection cannot be sustained for the reasons given above for the three primary references. The additional reference, Noda, was cited as disclosing controlled-release formulations but does not provide any motivation or reasonable expectation of success for the combination of an NPY receptor agonist and an agonist for a $5HT_6$ receptor. Consequently, this rejection may now also be withdrawn.

Conclusion

This application presents allowable subject matter and the Examiner is respectfully requested to pass it to issue. The Examiner is kindly invited to contact the undersigned should a further discussion of the issues or claims be helpful.

Respectfully submitted,

OBLON, SPIVAK, McCLELLAND,
MAIER & NEUSTADT, L.L.P.

Thomas M. Cunningham, Ph.D.
Registration No. 45,394

Customer Number
22850

Tel: (703) 413-3000
Fax: (703) 413 -2220
(OSMMN 07/09)